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EXHIBIT 1

00002

1 THE VIDEOGRAPHER: Good morning.
2 We are now on the record. My name is Katrina McCray,
3 videographer for Byers & Anderson Court Reporters
4 located at 600 University Street, Suite 2300 Seattle,
5 Washington, 98101.
6 Today is November 12th, 2001, and it is now 8:59
7 a.m. This is the videotaped deposition of Dr. David
8 Persing being taken in the case of Gen-Probe,
9 Incorporated, versus Vysis, Incorporated, Cause No.
10 99CV2668 H.
11 Today's deposition is being held at the law
12 offices of Coolly Godward in Kirkland, Washington.
13 Will the attorneys present please introduce
14 themselves for the record.
15 MR. BOWEN: William Bowen,
16 Gen-Probe, Incorporated, for plaintiff Gen-Probe,
17 Incorporated.
18 MR. LIPSEY: Charles Lipsey,
19 Finnegan, Henderson, Farabow, Garrett, & Dunner, for
20 the defendant Vysis and for the witness, Dr. Persing.
21 THE VIDEOGRAPHER: The court
22 reporter today is Barbara Hayden. You may swear in the
23 witness and proceed at this time.
24
25

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1 DAVID H. PERSING, M.D., Ph.D., having been first duly
2 sworn by the Notary,
3 deposed and testified as
4 follows:
5

6 MR. LIPSEY: Mr. Bowen, before we
7 get started, Gen-Probe served upon Dr. Persing on Friday
8 a subpoena seeking production of documents this morning.
9 Dr. Persing and Vysis object to the scope of the
10 subpoena as being unduly broad and encompassing material
11 that's burdensome to collect, that's irrelevant and
12 immaterial and not reasonably calculated to lead to the
13 discovery of admissible evidence.

14 We made an effort to locate documents reflecting
15 the materials that Dr. Persing had been sent or sent or
16 considered in formulating his opinions, and were able to
17 gather a stack of materials about two feet high which
18 we've given you here this morning, but would otherwise
19 object to responding to the subpoena.

20 MR. BOWEN: I'd like to mark as --

21 Q (By Mr. Bowen) Would you please state your name.

22 A David Persing.

23 Q Dr. Persing, I'd like you to look at what we will mark
24 as Exhibit 1 to your deposition, a subpoena in the case
25 of Gen-Probe versus Vysis. Have you seen Exhibit 1

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1 A (Witness reviews document.) I really can't comment any
2 further beyond what I've already said.

3 Q Can you tell me what your understanding is of the term
4 specific amplification?

5 A Specific amplification is a process whereby nucleic
6 acids are amplified from a target template using a
7 combination of sequence specific oligonucleotide
8 primers, and during the amplification process both
9 target specific and nontarget specific templates are
10 co-amplified in the reaction.

11 But in a specific amplification process, what we
12 call specific in the field of molecular diagnostics,
13 there is a general enrichment for the target nucleotide
14 sequence in favor of nonspecific amplification products.
15 And so there tends to be an increase in the number of
16 needles in the needle in the haystack analogy where you
17 have a needle within a large haystack and trying to find
18 the needle. A specific amplification process would
19 generate more needles than hay straws, but there are
20 some hay straws that get generated in the process as
21 well.

22 Nonspecific amplification processes may also use
23 oligonucleotides within the amplification mixture, some
24 of which are sequence specific just by virtue of their
25 random sequence composition. And those oligonucleotides

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1 can initiate a sequence specific process, but in general
2 the accumulation of target, target within -- using the
3 needle in a haystack analogy accumulation of the number
4 of needles is in proportion to the rest of the haystack.
5 And so there isn't as much if any, general enrichment
6 for needles within the haystack.
7 So that's why target capture is useful, because
8 target capture can enrich for the needles prior to
9 amplification, and thus one can use a nonspecific as
10 well as a specific amplification process on the captured
11 needles, and the end result is the same. And in that
12 context, the specific and nonspecific amplification
13 processes are functioning equivalently.
14 Q I believe in a portion of your answer where you were
15 discussing specific amplification you said with respect
16 to specific amplification that the process in the field
17 results in general enrichment in favor of nonspecific
18 amplification products?
19 A If I said that I was mistaken. I said that both
20 specific and nonspecific amplification products are
21 generated during even what we call a specific
22 amplification reaction and that in many cases the
23 nonspecific amplification products can outnumber the
24 specific amplification products, but there's general
25 proportional enrichment for the target specific

1 sequences within what we call a specific amplification
2 process relative to the nonspecific amplification
3 products.

4 Q Towards the end of your answer you made a statement
5 about the benefit of target capture in connection with
6 both specific and nonspecific amplification.

7 Considering specific amplification and nonspecific
8 amplification without such a target capture step, is
9 nonspecific amplification substantially different from
10 specific amplification in your understanding?

11 MR. LIPSEY: Object to the form.

12 A Well, as I've stated in my expert report for the
13 purposes of this amplification when working with
14 purified template, both specific and nonspecific
15 amplification processes are capable of generating the
16 same net result.

17 MR. BOWEN: Objection. Move to

18 strike, not responsive.

19 Q (By Mr. Bowen) I'm asking you now, though, to consider
20 the methods without target capture. And I know that you
21 in your opinion have expressed views considering target
22 capture as a preliminary step, but I'd like to explore
23 with you, which I'm entitled to do, your views of the
24 methods without such a step. Vysis and Gen-Probe may
25 argue what the legal relevance of those questions are.

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1 But I'd like to explore and get your views on the
2 methods without a preliminary target capture step.
3 So my question to you is, if one was to practice
4 nonspecific amplification without a target capture step,
5 would it be substantially different than specific
6 amplification?
7 MR. LIPSEY: Object to the form,
8 lack of foundation, beyond the scope of his report.
9 A I don't think I can really comment on that based on my
10 involvement with this case and the material that I've
11 been exposed to. I think I might be stepping outside of
12 my bounds if I comment on that.
13 Q (By Mr. Bowen) So you don't have an opinion on whether
14 or not nonspecific amplification considered without a
15 target capture step is substantially different than
16 specific amplification?
17 A I think the target capture step is so -- and a target
18 enrichment step, whether it's target capture or any
19 other method, is so central to those amplification
20 techniques that I don't think it's worthy of
21 consideration outside of the sample preparation process.
22 Q Do you have any understanding that PCR is practiced
23 without a target capture step?
24 A Yes, I'm aware that that is one -- one way of performing
25 PCR.

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1 understanding is that for some sample types, TMA is a
2 viable diagnostic method without a target capture step?
3 A In sample types that already have a natural state of
4 enrichment of the target sequence, I think both TMA and
5 PCR perform better. The diagnostic result is more
6 accurate because of the lack of competing nucleic acids
7 within the sample.
8 Q The FDA has approved diagnostic kits using PCR and TMA
9 without a target capture step; is --
10 A Right.
11 Q -- that your understanding?
12 A Yes.
13 Q Has the FDA ever approved any nonspecific amplification
14 method using random hexamer primers that didn't
15 incorporate a target step?
16 MR. LIPSEY: Object to the form,
17 lack of foundation.
18 A Not to my knowledge.
19 Q (By Mr. Bowen) Has the FDA to the best of your
20 knowledge ever approved any assay that uses random
21 hexamer primers?
22 MR. LIPSEY: Same objection.
23 A I'm not sure, but I believe that some of the assays
24 based on RTPCR in which a template is first converted
25 from RNA to DNA may use random hexamer primers.

1 sequences in the sample, i.e., the ratio of target to
2 extraneous sequence is vastly increased." Closed quote.
3 A Okay.
4 Q Do you have an understanding of the word vastly when the
5 article was published?
6 A I would say it's equivalent to substantially,
7 substantially increased.
8 Q It's your understanding that methods of specific
9 amplification increase the ratio of target to the other
10 sequences in a sample; is that true?
11 A That's generally my opinion.
12 Q Nonspecific methods of amplification do not increase the
13 relative proportion of the target and the other
14 sequences in a sample; is that true?
15 MR. LIPSEY: Object to the form.
16 A It would depend on the nature of the nonspecific
17 amplification technique.
18 Q I'd like you to look at what we'll mark as Exhibit 9, a
19 document entitled declaration of Dr. David H. Persing in
20 support of Vysis's opposition to Gen-Probe's motion for
21 partial summary judgement. Is that your signature on
22 Page 8 of Exhibit 9?
23 A Yes, it is.
24 Q I'd like to you look please of Page 3, Paragraph 8, line
25 24. At the end of line 24 a sentence begins quote, that

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1 is because nonspecific amplification techniques amplify
2 all the nucleic acid in a sample, both target and
3 nontarget nucleic acid. End of quote.
4 A Yes.
5 Q That statement was true when you signed your
6 declaration?
7 A Yes, I would agree with that statement.
8 Q And the next sentence states, quote, specific
9 amplification techniques in contrast are intended to
10 amplify only the target nucleic acid. Do you see that?
11 A Yes.
12 Q That was true when you signed your declaration?
13 A Yes.
14 Q And that's a difference between nonspecific and specific
15 techniques, isn't it?
16 MR. LIPSEY: Object to the form.
17 A It's a difference in intent. It's not always a
18 difference in outcome.
19 Q (By Mr. Bowen) Without the use of target capture prior
20 to amplification, is nonspecific amplification a viable
21 technique for detecting nucleic acids in samples?
22 MR. LIPSEY: Object to form, lack of
23 foundation.
24 A Yes, I would say it would be a powerful method if the
25 input material from a clinical specimen is enriched for

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- 1 A Yes, it is in the context of the declaration, yes.
2 Q Do you understand here in the last sentence that you're
3 communicating to the Court your belief that without a
4 target capture step, nonspecific amplification can't be
5 used in an diagnostic assay?
6 MR. LIPSEY: Object to the form.
7 The document speaks for itself.
8 A It does, and I think I wouldn't want to go beyond my
9 declaration, the fact that the document spoke to the use
10 of a -- to applying to clinical specimens for which
11 there was a mixture of target and nontarget nucleic
12 acids and for which nonspecific amplification methods
13 would not be useful. And the specific example I just
14 gave you where nonspecific amplification are equivalent
15 to specific amplifications in their diagnostic utility
16 only pertains to certain types of specimens in which
17 there is natural enrichment for the target sequence, or
18 natural enrichment by virtue of biological amplification
19 of the material prior to analysis. So in a context of
20 this declaration, it is a correct statement.
21 Q Specific amplification makes more copies of the needle
22 in the haystack; is that true?
23 A Yes.
24 Q Nonspecific amplification makes copies of everything,
25 both the needle and the haystack is that true?

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1 A Specific amplification makes copies of the haystack as
2 well, but the proportion is lower of haystack to needle.
3 Q Specific amplification increases the relative proportion
4 of the needle in the haystack; is that true?
5 A I would say that's generally true.
6 Q Nonspecific amplification does not increase the relative
7 proportion of the needle in the haystack generally.
8 That's true; right?
9 A I think that's generally true.
10 Q Nonspecific amplification does not increase the amount
11 of a particular sequence relative to all other nucleic
12 acids in the sample; is that true?
13 A I think that's generally true.
14 Q Would you agree that when employed by one skilled in the
15 art, methods of sequence specific amplification are
16 extremely specific as compared with amplification using
17 random hexamer primers?
18 MR. LIPSEY: Object to the form.
19 A I can't really comment on that because it would depend
20 on the nature of the input target material, how pure the
21 target was.
22 Q (By Mr. Bowen) If the target input was a mixture of
23 nucleic acids in a human clinical sample, is it true
24 that specific amplification methods are extremely
25 specific as compared with random hexamer primer

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1 publication?
2 A I did, yeah.
3 Q Had you had any experience with the Gen-Probe amplified
4 tuberculosis assay as of 1997?
5 A No.
6 Q Were you aware that as of 1997 Gen-Probe had obtained
7 FDA approval for mycobacterium tuberculosis assay?
8 A Yes.
9 Q And did you have an understanding that was an assay that
10 used TMA amplification?
11 A That was my understanding.
12 Q And was it your understanding that that assay did not
13 have a target capture step?
14 A I wasn't aware of the details of the assay at that time.
15 Q Is it your understanding today that that assay does not
16 have a target capture step?
17 A I haven't used the assay so I can't -- can't speak to
18 that.
19 Q So you don't know whether Gen-Probe has obtained FDA
20 approval for TMA assays that don't include a target
21 capture step?
22 A I believe that they have, but I don't -- I can't speak
23 specifically to this instance.
24 Q Do you know what the clinical specificity of those
25 assays is?

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1 trying to get to your punch line.
2 A It will take me some time to go through this just to
3 make sure I'm not --
4 Q (By Mr. Bowen) Let's talk about Example 5.
5 A Okay. All right.
6 Q Do you see that in the first paragraph of Example 5 it
7 says, "in this example, both nonspecific replication of
8 target DNA and transcription of that DNA are used to
9 amplify?
10 A Yes.
11 Q Do you agree that this example describes nonspecific
12 replication of target DNA and transcription of that DNA?
13 MR. LIPSEY: May I hear the question
14 again, please?
15 (Question on Page ^ , Lines ^
16 through ^ , read by the
17 reporter.)
18
19 MR. LIPSEY: Object to the form.
20 A Yeah, I really can't -- can't comment there. I'm not
21 sure what the -- what the question is and what the --
22 Q (By Mr. Bowen) The question is, do you agree with the
23 statement there in the first sentence of Example 5 that
24 the example describes the use of nonspecific replication
25 of target DNA and transcription of that DNA?

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1 MR. LIPSEY: Object to the form.
2 A I think it does describe the use of oligohexamer primers
3 which would be able to initiate replication
4 nonspecifically, but it also contains a specific mention
5 of sequence specific primer extension. So, you know, I
6 don't know, I can't really comment beyond that except to
7 say it seems to comprise elements of both.
8 Q (By Mr. Bowen) Do you see in the second paragraph of
9 Example 5 there's a reference to Figure 5?
10 A Okay.
11 Q Would you look at Figure 5, which is at the front of the
12 packet, please?
13 A Okay. Mm-hm.
14 Q Figure 5 describes the use of capture probe as a primer;
15 is that your understanding?
16 MR. LIPSEY: Object to the form.
17 A (Witness reviews document.) Yes, I think in general
18 terms it does describe use of a capture technique or
19 sequence enrichment.
20 Q I'd like you to look please at Column 31 of the patent.
21 Oops. I think I just did that wrong. I did. I'm
22 sorry. Column 15. In Column 15, the left-hand column
23 starting about Line 56, do you see that it says, "In
24 Step 3 of Figures 4, 5 and 6 the isolated target is
25 non-specifiably" -- I think that should probably be

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1 nonspecifically -- "amplified to form a multitude of
2 amplification products"?

3 A Okay. That's -- I agree that's what it -- that's what
4 it reads.

5 Q And do you agree that figure -- that in Figure 5 the
6 isolated target is nonspecifically amplified?

7 A Well, it's confusing because Example 5 does -- recites
8 Figure 5, does specify the double-stranded DNA being
9 used -- being captured specifically with a probe, and
10 then the synthesis can start from the capture probe. So
11 in that sense the initial steps of the amplification
12 process are indeed specific. So it seems that there is
13 a -- sort of a disconnect between the Example 5 and
14 what's in Figure 5 and also what's in the content on the
15 passage that you just read.

16 Q You said that the initial steps of the amplification
17 process are specific if the capture probe is used as
18 primer. Is the overall process described in Example 5
19 if the capture probe is used as a primer, specific
20 amplification?

21 A I can't really comment on that. I think it comprises
22 elements of specificity and of nonspecificity as do many
23 amplification techniques.

24 Q I'd like you to look at what we will mark as Exhibit 14,
25 which is an excerpt from the deposition of Jonathon

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1 constitute amplification?

2 A I can't really say without seeing the Vary patent. I

3 would just again say that the initial primer extension

4 process is the initiating step in the amplification

5 process and it may be it may require several rounds of

6 primer extension initiation in a linear fashion before

7 the amplification process kicks in to gear efficiently.

8 Now, if -- that's all I really can say, is that the

9 primary extension I think is critical step -- sequence

10 specific primer extension is a critical step in

11 initiating amplification. In fact, I say right here,

12 "For example, amplification of nucleic acids by the

13 polymerase chain reaction follows primer extension with

14 separation of the double-stranded primer extension

15 product into single-stranded polynucleotides and

16 repeating the process steps."

17 So basically I again there point out that the

18 primer extension is the initiating event within the

19 amplification reaction.

20 Q Considering Example 5 and the use of the capture probe

21 as the point to begin synthesis, is it your

22 understanding that the replicated DNA resulting from

23 that process would be nonspecific in size?

24 A Could be.

25 Q Is it your understanding --